effective to elicit an immune response. The antibodies can be IgM, IgG, subtypes, IgG2a, IgG1, etc. Antibodies, and immune responses, can also be generated by administering naked DNA. See, e.g., U.S. Pat. Nos. 5,703,055; 5,589,466; 5,580,859.

Polypeptides for use in the induction of antibodies do not need to have biological activity; however, they must have immunogenic activity, either alone or in combination with a carrier. Peptides for use in the induction of specific-for antibodies may have an amino sequence consisting of at least five amino acids, preferably at least 10 amino acids. Short stretches of amino acids, e.g., five amino acids, can be fused with those of another protein such as keyhole limpet hemocyanin, or another useful carrier, and the chimeric molecule used for antibody production. Regions of PI3K useful in making antibodies are mentioned above and in the examples below.

The polypeptides and antibodies of the present invention may be used with or without modification. Frequently, the polypeptides and antibodies will be labeled by joining them, either covalently or noncovalently, with a substance which provides for a detectable signal. A wide variety of labels and conjugation techniques are known and have been reported extensively in both the scientific and patent literature. Suitable labels include radionuclides, enzymes, substrates, cofactors, inhibitors, fluorescent agents, chemiluminescent agents, magnetic particles and the like. Patents teaching the use of such labels include U.S. Pat. Nos. 3,817,837; 3,850,752; 3,939,350; 3,996,345; 4,277,437; 4,275,149; and 4,366,241.

Antibodies and other ligands which bind PI3K can be used in various ways, including as therapeutic, diagnostic, and commercial research tools, e.g., to quantitate the levels of Pi3k polypeptide in animals, tissues, cells, etc., to identify the cellular localization and/or distribution of it, to purify it, or a polypeptide comprising a part of it, to modulate the function of it, in Western blots, ELIZA, immunoprecipitation, RIA, etc. The present invention relates to such assays, compositions and kits for performing them, etc.

In addition, ligands which bind to a PI3K according to the present invention, or a derivative thereof, can also be prepared, e.g., using synthetic peptide libraries or aptamers (e.g., Pitrung et al., U.S. Pat. No. 5,143,854; Geysen et al., J. Immunol. Methods, 102:259-274, 1987; Scott et al., Science, 249:386, 1990; Blackwell et al., Science, 250:1104, 1990; Tuerk et al., 1990, Science, 249: 505.).

A polypeptide of the present invention can be combined with one or more structural domains, functional domains, detectable domains, antigenic domains, and/or a desired polypeptide of interest, in an arrangement which does not occur in nature, i.e., not naturally-occurring. A polypeptide comprising such features is a chimeric or fusion polypeptide. Such a chimeric polypeptide can be prepared according to various methods, including, chemical, synthetic, quasi-synthetic, and/or recombinant methods. A chimeric nucleic acid coding for a chimeric polypeptide can contain the various domains or desired polypeptides in a continuous (e.g., with multiple N-terminal domains to stabilize or enhance activity) or interrupted open reading frame, e.g., containing introns, splice sites, enhancers, etc. The chimeric nucleic acid can be produced according to various methods. See, e.g., U.S. Pat. No. 5,439,819. A domain or desired polypeptide can possess any desired property, including, a biological function such as signaling, growth promoting, cellular targeting (e.g., signal sequence, targeting sequence, such as targeting to the endoplasmic reticulum or nucleus), etc., a structural function such as hydrophobic, hydrophilic, membrane-spanning, etc., receptor-ligand functions, and/or detectable functions, e.g., combined with enzyme, fluorescent polypeptide, green fluorescent protein, (Chalfie et al., *Science*, 263:802, 1994; Cheng et al., *Nature Biotechnology*, 14:606, 1996; Levy et al., *Nature Biotechnology*, 14:610, 1996), etc. In addition, a polypeptide, or a part of it, can be used as a selectable marker when introduced into a host cell. For example, a nucleic acid coding for an amino acid sequence according to the present invention can be fused in-frame to a desired coding sequence and act as a tag for purification, selection, or marking purposes. The region of fusion can encode a cleavage site to facilitate expression, isolation, purification, etc.

A polypeptide according to the present invention can be produced in an expression system, e.g., in vivo, in vitro, cell-free, recombinant, cell fusion, etc., according to the present invention. Modifications to the polypeptide imparted by such systems include glycosylation, amino acid substitution (e.g., by differing codon usage), polypeptide processing such as digestion, cleavage, endopeptidase or exopeptidase activity, attachment of chemical moieties, including lipids and phosphates, etc.

EXAMPLES

We have determined the structure of the catalytic subunit (residues 144-1102) of porcine PI3Kγ. This construct contains all of the homology regions found in class I PI3Ks (HR1, HR2, HR3 and HR4) and has a catalytic activity similar to the full length enzyme. The N-terminal region absent in our construct of PI3Kγ is important for interaction with the p101 adaptor (5), and the analogous region of PI3Kα interacts with the p85 adaptor. The enzyme has a modular structure consisting of four domains: a Ras-binding domain (RBD), a C2 domain, a helical domain and a catalytic domain (Fig. 1). The RBD, C2 and catalytic domains have folds similar to these modules in other proteins involved in signal transduction. The helical domain has a fold akin to HEAT-repeat containing structures involved in protein-protein interactions.

The catalytic domain of the enzyme consists of a smaller N-terminal lobe (residues 726-883) and a larger C-terminal lobe (884-1092). The portion of the N-terminal lobe from kβ3 to kα3 and the first part of the C-terminal lobe (up to the end of kβ10) have a fold similar to protein kinases (reviewed in (6)), and this similarity extends to many of the details of the ATP binding site (Fig. 2). This region is among the most conserved regions of the PI3Ks (Fig. 3). The structural similarity of PI3K to protein kinases is consistent with finding that PI3Ks have a protein kinase activity in addition to their lipid kinase activities (7,8). The sequence alignment in Fig. 3 illustrates the regions of the enzyme that structurally superimpose with tyrosine protein kinase c-Src. The N-terminal lobe consists of a five-stranded antiparallel β-sheet flanked on one side by a helical hairpin (kα1-kα2) and a small two-stranded β-sheet (β1-β2) and on the other side by the kα3 helix and the C-terminal lobe. Strands